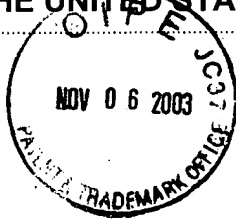


## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Liu, et al.



Serial No. 09/601,582

Filed: December 4, 2000

For: NOVEL GABAB RECEPTOR DNA SEQUENCES

Art Unit: 1646Examiner: Kaufman

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

**INFORMATION DISCLOSURE STATEMENT  
UNDER 37 CFR 1.97**

Sir:

1. In compliance with 37 C.F.R. 1.97, submitted on the attached form herewith is a list of patents, publications or other information which are requested to be made of record in this application. This Information Disclosure Statement is not an admission that any patent, publication or other information referred to herein is "prior art" for this invention. In accordance with 37 C.F.R. 1.97(h), the filing of this Information Disclosure Statement shall not be construed to be an admission that the information cited in the Statement is, or is considered to be, material to patentability as defined in 37 C.F.R. 1.56(b).

2. In accordance with 37 C.F.R. 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made.

3. Applicants respectfully request that the Examiner initial the attached form after reviewing the pertinence of each reference.

4. Pursuant to the waiver by the Office of the requirement under 37 CFR 1.98 (a)(2)(i) dated July 11, 2003, if the filing date of this application is after June 30, 2003, copies of each cited U.S. patent and each U.S. patent application publication are not enclosed herewith.

11/07/2003 SDIRETA1 00000096 132755 09601582

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date appearing below.

MERCK &amp; CO., INC.

By *Francis J. [Signature]* Date *Nov. 3, 2003*



# INFORMATION DISCLOSURE STATEMENT

5. Pursuant to 37 C.F.R. 1.98(d), copies of references listed on the attached form that were submitted to or cited by the Office in a related application upon which the instant application relies for an earlier filing date under 35 U.S.C. 120 are not enclosed. Related application(s) in which references were submitted to or cited by the Office are as follows:

RELATED APPLICATION		
U. S. SERIAL NUMBER	FILING DATE	MERCK CASE

If this is inconvenient, additional copies will be submitted upon request.

6. In accordance with 37 C.F.R. 1.97, (check one)

- ☐ the attached information is filed within three months of the filing date of the captioned case.
- ☐ the attached information is filed more than three months after the filing date but prior to the mailing of a first Office Action on the merits.
- ☒ the attached information is being filed more than three months after the filing date and after the mailing of a first Office Action on the merits, but before the mailing date of a Final Action or Notice of Allowance. The enclosed authorization is therefore given to charge Deposit Account No. 13-2755 for the fee required under 37 C.F.R. 1.17(p).
- ☐ the undersigned certifies that each item of information contained in this Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of this Statement.
- ☐ the undersigned certifies that no item of information contained in this Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, was known to any individual designated under 37 C.F.R. 1.56(c) more than three months prior to the filing of this Statement.

Respectfully submitted,

By: Vineet Kohli

Attorney \_\_\_\_\_ For Applicant(s)

Reg. No. 37,003

MERCK & CO., INC.

Patent Dept., RY60-30

P.O. Box 2000

Rahway, N.J. 07065-0907

(732)594-3889

Date: November 4, 2003

# FEE TRANSMITTAL

NOV 06 2003

Patent fees are subject to annual revision.

## Complete if Known

Application Number	09/601,582
Filing Date	December 4, 2000
First Named Inventor	Liu, et al.
Examiner Name	Kaufman
Group Art Unit	1646
Attorney Docket Number	20052YP

TOTAL AMOUNT OF PAYMENT \$180

## METHOD OF PAYMENT

☒ Deposit Account

Deposit Account Number   
Deposit Account Name

The Director is authorized to:

- ☒ Charge fee(s) indicated below ☒ Credit any overpayments  
☒ Charge any additional fee(s) during the pendency of this application

## FEE CALCULATION

### 1. BASIC FILING FEE

Large Fee Code	Entity Fee (\$)	Fee Description	Fee Paid
1001	770	Utility filing fee	
1002	340	Design filing fee	
1004	770	Reissue filing fee	
1005	160	Provisional filing fee	
SUBTOTAL(1)			\$0

### 2. EXTRA CLAIM FEES

	Extra	Fee from below	Fee Paid
Total Claims <input type="text" value="20"/>	** = <input type="text" value="0"/>	x \$18 =	<input type="text" value="0"/>
Independent Claims <input type="text" value="3"/>	** = <input type="text" value="0"/>	x \$86 =	<input type="text" value="0"/>
Multiple Dependent Claims		\$290 =	

\*\*or number previously paid, if greater; For Reissues, see below

Large Fee Code	Entity Fee (\$)	Fee Description
1202	18	Claims in excess of 20
1201	86	Independent claims in excess of 3
1203	290	Multiple dependent claim, if not paid
1204	86	**Reissue independent claims over original patent
1205	18	**Reissue claims in excess of 20 and over original patent

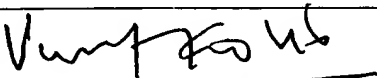
SUBTOTAL(2) \$0

### 3. ADDITIONAL FEES

Fee Code	Large Entity Fee (\$)	Fee Description	Fee Paid
1051	130	Surcharge - late filing fee or oath	
1812	2,520	For filing a request for <i>ex parte</i> reexamination	
1251	110	Extension for reply within first month	
1252	420	Extension for reply within second month	
1253	950	Extension for reply within third month	
1254	1,480	Extension for reply within fourth month	
1255	2,010	Extension for reply within fifth month	
1401	330	Notice of Appeal	
1402	330	Filing a brief in support of an appeal	
1403	290	Request for oral hearing	
1452	110	Petition to revive - unavoidable	
1453	1,330	Petition to revive - unintentional	
1501	1,330	Utility issue fee (or reissue)	
1502	480	Design issue fee	
1460	130	Petitions to the Commissioner	
1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	Submission of Information Disclosure Statement	180
8021	40	Recording each patent assignment per property (times number of properties)	
1809	770	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	770	For each additional invention to be examined (37 CFR 1.129(b))	
1801	770	Request for Continued Examination (RCE)	
Other fee (specify) _____			
Other fee (specify) _____			
SUBTOTAL(3)			\$180

## SUBMITTED BY

## Complete (if applicable)

Typed or Printed Name	Vineet Kohli	Reg. Number	37,003
Signature		Date	11/04/2003
		Deposit Account User ID	

Application Number: 09/601,582  
Filing Date: 12/04/2000  
First Named Inventor: Liu, et al.  
Group Art Unit: 1646  
Examiner Name: Kaufman  
Attorney Docket Number: 20052YP

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**FIRST CLASS MAIL CERTIFICATE**

I HEREBY CERTIFY THAT THIS CORRESPONDENCE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL IN AN ENVELOPE ADDRESSED TO: COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VIRGINIA 22313-1450, ON THE DATE APPEARING BELOW.

**MERCK & CO., INC.**

MAILED BY *Nancy Elzner* DATE *Nov. 3, 2003*

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DISCLOSURE

APPLICANT

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as necessary)

TRADEMARK OFFICE

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of

6

Attorney Docket Number	20052YP
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Substitute for form 1449B/PTO <b>INFORMATION DISCLOSURE</b> <b>STATEMENT BY APPLICANT</b> <i>(use as many sheets as necessary)</i>			<b>COMPLETE IF KNOWN</b>		
			Application Number	09/601,582	
			Filing Date	December 4, 2000	
			First Named Inventor	Liu, et al.	
			Group Art Unit	1646	
			Examiner Name	Kaufman	
Sheet	2	of	6	Attorney Docket Number	20052YP

NON PATENT LITERATURE DOCUMENTS		
Examiner Initials*	Cite No.	Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.
✓		Altschul, et al., "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", Nucleic Acids Research", Vol. 25, No. 17, 1997.
✓		Amatruda, et al., "Specific Interactions of Chemoattractant Factor Receptors with G-proteins*", The Journal of Biological Chemistry", Vol. 268, No. 14, pp. 10139-10144, May 15, 1993.
✓		Andrade, et al., "A G Protein Couples Serotonin and GABAB Receptors to the Same Channels in Hippocampus", Vol. 234, pp. 1261-1265, 1986.
✓		Blakely, et al., "Vaccinia-T7 Polymerase Expression System: Evaluation for the Expression Cloning of Plasma Membrane Transporters", Analytical Biochemistry, Vol. 194, pp. 302-308, 1991.
✓		Bormann & Feigenspan, "GABAC Receptors", Trends Neurosci., Vol. 18, pp. 515-518, 1995.
✓		Bowery, et al., "GABAB receptors and their significance in mammalian pharmacology", Trends in Pharmacological Sciences, Vol. 10, No. 10, pp. 401-407, 1989.
✓		Bowery & Pratt, "GABAB Receptors as Targets for Drug Action", Arzneim.-Forsch/Drug Res., Vol. 42, pp. 215-223, 1992.
✓		Bradley, et al., "Spacial and Temporal Expression of alpha- and beta-Thyroid Hormone Receptor mRNAs, Including the beta-2-Subtype, in the Developing Mammalian Nervous System", J. of Neurosci., Vol. 12, pp. 2288-2302, 1992.
✓		Brakeman, et al., "Homer: a protein that selectively binds metabotropic glutamate receptors", Nature, Vol. 386, pp. 284-288, 1007.
✓		Brooker, et al., "Advances in Cyclic Nucleotide Research", Adv. Cyclic Nucleic Research, Vol. 10, pp. 1-33, 1979.
✓		Chou & Heinrikson, "Prediction of the Tertiary Structure of the Complement Control Protein Module", Journal of Protein Chemistry, Vol. 16, pp. 765-773, 1997.
✓		Clark, et al., "Multiple Regions of Ligand Discrimination Revealed by Analysis of Chimeric Parathyroid Hormone 2 (PTH2) and PTH/PTH-Related Peptide (PTHrP) Receptors", Molecular Endocrinology, Vol. 12, pp. 193-206, 1998.
✓		Couve, et al., "Intracellular Retention of Recombinant GABAB Receptors", J. Biol. Chem., Vol. 273, pp. 26361-26367, 1998.
✓		Cunningham & Wells, "High-Resolution Epitope Mapping of hGH-Receptor Interactions by Alanine Scanning Mutagenesis", Science, Vol. 244, pp. 1081-1085 (1989).
✓		Gahwiler, et al., "GABAB-receptor-activated K <sup>+</sup> current in voltage-clamped CA3 pyramidal cells in hippocampal cultures", Proc. Natl. Acad. Sci., Vol. 82, pp. 1558-1562, 1985.

Examiner Signature		Date Considered	
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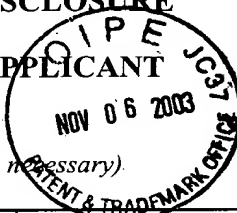
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## **COMPLETE IF KNOWN**

Application Number	09/601,582
Filing Date	December 4, 2000
First Named Inventor	Liu, et al.
Group Art Unit	1646
Examiner Name	Kaufman
Attorney Docket Number	20052YP

Sheet	3	of	6
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## **NON PATENT LITERATURE DOCUMENTS**

Examiner Initials*	Cite No.	Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.
/		Gonzalez & Tsien, "Voltage Sensing by Fluorescence Resonance Energy Transfer in Single Cells", Biophysical Journal, Vol. 69, pp. 1272-1280, 1995.
/		Gonzalez & Tsien, "Improved indicators of cell membrane potential that use fluorescence resonance energy transfer", Chemistry & Biology, Vol. 4, pp. 269-277, 1997.
/		Graminski, et al., "Pigment Dispersion in Grog Malanophores Can Be Induced by a Phorbol Ester or Stimulation of a Recombinant Receptor That Activates Phospholipase C", J. Biol. Chem., Vol. 268, pp. 5957-5967, 1993.
/		Guan, et al., "Enhancement of Membrane Insertion and Function in a Type IIIb Membrane Protein following Introduction of a Cleavable Signal Peptide", J. Biol. Chem., Vol. 267, pp. 21995-21998, 1992.
/		Hebert, et la., "A Peptide Derived from a + 2-Adrenergic Receptor Transmembrane Domain Inhibits Both Receptor Dimerization and Activation", J. Biol. Chem., Vol. 271, pp. 16384-16392, 1996.
/		Hess, et al., "Cloning and Pharmacological Characterization of a Human Bradykinin (BK-2) Receptor", Biochem. and Biophy. Res. Comm., Vol. 184, No. 1, pp. 260-268, 1992.
/		Hodgson, "Receptor Screening and the Search for New Pharmaceuticals", Bio/Technology, Vol. 10, pp. 973-980, 1992.
/		Hopp & Woods, "Prediction of protein antigenic determinants from amino acid sequences", Proc. Natl. Acad. Sci. USA, Vol. 78, No. 6, pp. 3824-2828, June 1981.
/		Howard, et al., "A Receptor in Pituitary and Hypothalamus That Functions in Growth Hormone Release", Science, Vol. 273, pp. 974-977, 1996.
/		Jameson, et al., "The antigenic index: a novel algorithm for predicting antigenic determinants", BABIOS, Vol. 4, No. 1, pp. 181-186, 1988.
/		Kohler & Milstein, "Continuous cultures of fused cells secreting antibody of predefined specificity", Nature, Vol. 256, pp. 495-497, 1975.
/		Kolakowski, et al., "ProSearch: Fast Searching of Protein Sequences with Regular Expression Patterns Related to Protein Structure and Function", BioTechniques, Vol. 13, No. 6, pp. 919-921, 1992.
/		Lerner, "Tols for investigating functional interactions between ligands and G-protein-coupled receptors", Trends Neurosci., Vol. 17, pp. 142-146, 1994.
/		Lofts, et al., "Specific short transmembrane sequences can inhibit transformation by the mutant neu growth factor receptor in vitro and in vivo", Oncogene, Vol. 8, pp. 2813-2820, 1993.
/		Maidment, et al., "Microdialysis of Extracellular Endogenous Opioid Peptides From Rat Brain In Vivo", Neuroscience, Vol. 33, No. 3, pp. 549-557, 1989.

Examiner Signature	Date Considered
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			First Named Inventor	Liu, et al.	
			Group Art Unit	1646	
			Examiner Name	Kaufman	
Sheet	4	of	6	Attorney Docket Number	20052YP


NON PATENT LITERATURE DOCUMENTS		
Examiner Initials*	Cite No.	Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.
/		McKee, et al., "Molecular Analysis of Rat Pituitary and Hypothalamic Growth Hormone Secretagogue Receptors", Molecular Endocrinology, Vol. 11, pp. 415-423, 1997.
/		McKernan & Whiting, "Which GABAA-receptor subtypes really occur in the brain?", Trends Neurosci., Vol. 16, pp. 139-143, 1996.
/		Misgeld, et al., "A Physiological Role for GABAB Receptors and the Effects of Baclofen in the Mammalian Central Nervous System", Vol. 46, pp. 423-462, 1995.
/		Ng, et al., "Dopamine D2 Receptor Dimers and Receptor-Blocking Peptides", Biochemical and Biophysical Research Communications, Vol. 227, pp. 200-204, 1996.
/		Nicholson, et al., "The gene for hereditary sensory neuropathy type 1 (HSN-1) maps to chromosome 9q22.1-122.3", Nature Genetics, Vol. 12, pp. 101-104, 1996.
/		North, "Twelfth Gaddum Memorial Lecture", Br. J. Pharmacol., Vol. 98, pp. 13-28, 1989.
/		Buhl, et al., "Selective coupling of the human anaphylatoxin C5a receptor and alpha 16 in human kidney 293 cells", FEBS Lett., Vol. 323, No. 1, 2, pp. 132-132, 1993.
/		Offermanns, et al., "Alpha15 and Alpha16 Couple a Wide Variety of Receptors to Phospholipase C", J. Biol. Chem., Vol. 270, No. 28, pp. 15175-15180, 1995.
/		O'Hara, et al., "The Ligand-Binding Domain in Metabotropic Glutamate Receptors Is Related to Bacterial Periplasmic Binding Proteins", Neuron, Vol. 11, pp. 41-52, 1993.
/		Pearson, et al., "Comparison of DNA Sequences with Protein Sequences", Genomics, Vol. 46, pp. 24-36, 1997.
/		Perkins, et al., "A Study of the Structure of Human Complement Component Factor H by Fourier Transform Infrared Spectroscopy and Secondary Structure Averaging Methods", Vol. 27, pp. 4004-4012, 1988.
/		Pin and Duvoisin, "Review: Neurotransmitter Receptors I The Metabotropic Glutamate Receptors: Structure and Functions", Neuropharmacology, Vol. 14, No. 1, pp. 1-23, 1995.
/		Potenza & Lerner, "A Rapid Quantitative Bioassay for Evaluating the Effects of Ligands Upon Receptors That Modulate cAMP Levels in a Melanophore Cell Line", Pigment Cell Research, Vol. 5, pp. 372-375, 1992.
/		Potenza, et al., "A Method for Evaluating the Effects of Ligands upon G3 Protein-Coupled Receptors Using a Recombinant Melanophore-Based Bioassay", Analytical Biochemistry, Vol. 206, pp. 315-322, 1992.
/		Romano, et al., "Metabotropic Glutamate Receptor 5 Is A Disulfide-linked Dimer", J. Biol. Chem., Vol. 271, No. 45, pp. 28612-28616, 1996.

Examiner Signature	Date Considered
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			Application Number	09/601,582	
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			First Named Inventor	Liu, et al.	
			Group Art Unit	1646	
			Examiner Name	Kaufman	
Sheet	5	of	6	Attorney Docket Number	20052YP

NON PATENT LITERATURE DOCUMENTS		
Examiner Initials*	Cite No.	Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.
/		Rutter, et al., "Real-time imaging of gene expression in single living cells", Chemistry & Biology, Vol. 5, pp. R285-R290, 1998.
/		Sequier, et al., "Mapping of brain areas containing RNA homologous to cDNAs encoding the alpha and beta subunits of the rat GABAA gamma-aminobutyrate receptor", Proc. Natl. Acad. Sci. USA, Vol. 85, pp. 7815-7819, October 1988.
/		Watson, et al., "The Fine Structure of Bacterial and Phage Genes", Molecular Biology of the Gene", Fourth Edition, The Benjamin/Cummings Press, pp. 214-238, 1987.
/		White, et al., "Heterodimerization is required for the formation of a functional GABAB receptor", Nature, Vol. 396, pp. 679-682, 1998.
/		Yokomizo, et al., "A G-protein-coupled receptor for leukotriene B4 that mediates chemotaxis", Nature, Vol. 387, pp. 620-624, 1997.
/		Zlokarnik, et al., "Quantitation of Transcription and Clonal Selection of Single Living Cells with Beta-Lactamase as Reporter", Science, Vol. 279, pp. 87-88, 1988.
/		GenBank Accession No. Y10369
/		GenBank Accession No. Y11044
/		GenBank Accession No. Y10370
/		GenBank Accession No. AJ012188
/		GenBank Accession No. 3776096
/		GenBank Accession No. AF074483
/		GenBank Accession No. AF056085
/		GenBank Accession No. AJ012185
/		GenBank Accession No. Y10369

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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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**COMPLETE IF KNOWN**

<b>Application Number</b>	09/601,582
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<b>Filing Date</b>	December 4, 2000
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<b>First Named Inventor</b>	Liu, et al.
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Group Art Unit	1646
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Examiner Name	Kaufman
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Attorney Docket Number	20052YP
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Sheet

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of

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## NON PATENT LITERATURE DOCUMENTS

Examiner  
Initials\*Cite  
No.

**Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.**

GenBank Accession No. H14151

GenBank Accession No. Z43654

GenBank Accession No. T07621

Kaupmann, et al., "Expression cloning of GABAB receptors uncovers similarity to metabotropic glutamate receptors", *Nature*, Vol. 386, pp. 239-246, 1997

Kaupmann, et al., "GABAB-receptor subtypes assemble into functional heteromeric complexes", *Nature*, Vol. 396, pp.683-687, 1998.

Jones, et al., "GABAB receptors function as a heteromeric assembly if the subunits GABABR1 and GABABR2", *Nature*, Vol. 396, pp. 674-678, 1998.

Kuner, et al., "Role of Heteromer Formation in GABAB Receptor Function", *Science*, Vol. 283, pp. 74-77, 1999.

Examiner  
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